SUMMARY OF INTERVIEW

Identification of Claims Discussed

All of the pending claims were discussed.

Principal Arguments and Other Matters

Applicant's representatives discussed the pending Office Action and the issues raised by the Examiner with regard to the written description rejection. Applicant's representatives argued that the pending claims met the written description requirements of 35 U.S.C. §112. Applicant's representatives proposed replacing the term "non-cleaving" with "non-catalytic" or "non-enzymatic, and replacing the term "compound" with "oligonucleotide."

Results of Interview

No agreement was reached with the Examiner with regards to the issues presented in the pending Office Action. The Examiner noted that replacing the term "non-cleaving" with "non-catalytic" or "non-enzymatic, and replacing the term "compound" with "oligonucleotide," would obviate the 35 U.S.C. §112, 1st paragraph rejection of record.

REMARKS

Applicant wishes to thank Examiner Epps-Ford for the courteous personal interview conducted on November 2, 2005 to discuss the issues raised by the Office Action mailed October 4, 2005. Claims 15-19 are withdrawn. Claims 1, 4, 5, 8-12, and 20 have been amended. Support for the claim amendments can be found throughout the specification. Claims 2-3, 6-7, 14, and 21-27 are canceled. Newly introduced Claims 30-39 find support throughout the specification. As described below in detail, support for the use of "start codon region" in amended Claim 1 and nucleotide ranges in newly introduced claims 29-32 can be found on page 9, lines 10-14, and in the sequence listing as filed. Accordingly, following entry of the amendments submitted herewith, Claims 1, 4, 5, 8-13, 20, 28, and 30-39 are pending. No new matter has been added by way of these amendments. Reconsideration of the pending claims in view of the amendments and comments presented herein is respectfully requested.

Discussion of Rejection Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1, 11, 20 and 28 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully disagree. However, solely in an effort to advance prosecution, Applicant has amended claims 1, 11, and 20 to replace "non-cleaving" with "non-catalytic" and to replace "compound" with "oligonucleotide compound". This amendment obviates the rejection and therefore Applicant respectfully requests that it be withdrawn.

Discussion of Rejection Under 35 U.S.C. §102

The Examiner rejected claims 1-2, 4-5, 11-12, 14 and 20 under 35 U.S.C. §102(b) as being anticipated by Tang et al., who allegedly disclose an antisense compound that is 20 nucleotides in length targeting nucleotides 129 through 148 of SEQ ID NO: 3. The Examiner argues that the structure of the antisense compound disclosed by Tang et al. meets the structural limitations recited in the instant claims.

In an effort to advance prosecution of the claims, independent claims 1 and 11 have been amended such that non-catalytic oligonucleotide compounds targeted to the start codon of SEQ ID NO: 3 are excluded from the genus of non-catalytic oligonucleotide compounds encompassed

by these claims. Support for the amendments to Claims 1 and 11 and for newly introduced Claims 31 and 32 is found in the specification as filed. For example, the specification defines the "start codon region" as encompassing from about 25 to about 50 contiguous nucleotides in the 5' or 3' direction from a translation initiation codon (see page 9, lines 10-14). As illustrated on page 1 of the sequence listing as filed, the translation initiation codon of SEQ ID NO: 3 is found at nucleotides 129-131. In view of the above definition, one specifically-described "start codon region" for SEQ ID NO: 3 begins 50 nucleotides in the 5' direction from the translation initiation codon (i.e., at nucleotide 79, which is 50 nucleotides upstream of nucleotide 129 of SEQ ID NO: 3) and ends 50 nucleotides in the 3' direction from the translation initiation codon (i.e. at nucleotide 181, which is 50 nucleotides downstream from nucleotide 131 of SEQ ID NO: 3). As such, the specification adequately describes the "start codon region" for SEQ ID NO: 3 as being found at nucleotides 79-181. Another specifically-described "start codon region", begins and ends 25 nucleotides in the 5' and 3' directions, respectively, from the translation initiation codon. Applying the same calculus as described above, this region can be found at nucleotides 104 to 156 of SEQ ID NO: 3. Thus, the limitation "non-catalytic oligonucleotide compounds not targeted to the start codon region of SEQ ID NO: 3" includes non-catalytic oligonucleotide compounds targeted to nucleotides 1 to 103 or 157 to 14121 of SEQ ID NO: 3, as claimed in dependent claim 31. Further, the limitation "non-catalytic oligonucleotide compounds not targeted to the start codon region of SEQ ID NO: 3" includes non-catalytic oligonucleotides targeted to nucleotides 1 to 79 or 182 to 14121 of SEQ ID NO: 3, as claimed in dependent claim 32.

In view of the above-described amendments, non-catalytic oligonucleotide compounds targeted to the start codon of SEQ ID NO: 3 are excluded from the genus of non-catalytic oligonucleotide compounds encompassed by Claims 1 and 11. The portion of SEQ ID NO: 3 targeted by the antisense compound disclosed by Tang et al. is encompassed by the term "start codon region". Accordingly, the antisense compound disclosed by Tang et al. does not meet the structural limitations of amended Claim 1, 11 or of any of the newly introduced Claims. Furthermore, none of the claimed non-catalytic oligonucleotide compounds would be obvious in view of Tang et al., as one of ordinary skill in the art, upon reviewing the disclosure of Tang et al., would not have a reasonable expectation of success in making the oligonucleotide

compounds as claimed, as described below. Thus, these amendments obviate the rejection of claims 1-2, 4-5, 11-12, 14 and 20 under 35 U.S.C. §102(b) and Applicant respectfully requests that the rejection be withdrawn.

Discussion of Rejection Under 35 USC § 103

The Examiner rejected Claims 1-2, 4-14, 20, and 28 under 35 U.S.C. 103(a) as being unpatentable over Tang et al. in view of Cowsert (U.S. Patent No. 5,945,290). Applicant respectfully disagrees.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The Examiner argues that "one of ordinary skill in the art would have been motivated to modify the antisense compound and compositions of Tang et al." with the teachings of Cowsert in the design of the instant invention. However, one of ordinary skill in the art does not have a reasonable expectation of success at generating the non-catalytic oligonucleotide compounds encompassed by the instant claims simply because Cowsert purportedly discloses methods for modifying antisense compounds. Moreover, Tang et al. in their discussion state that "from the perspective of the empirical inhibition percentage, the results were not very ideal", and that "the less than ideal inhibition rate was also very likely related to an inadequate AODN concentration". In contrast to the teachings of Tang et al., Applicant has discovered numerous examples of oligonucleotide compounds that result in reductions of apolipoprotein B mRNA levels of at least 70% (see Table 1). As described in the instant specification, these oligonucleotide compounds are capable of eliciting inhibition of apolipoprotein B mRNA at levels approximately 2.5 times greater than that achieved by Tang et al., using a concentration of oligonucleotide compound approximately 33 times lower than that employed by Tang et al. (i.e. the inhibition and concentration required by the instant claims). Thus, based upon the disclosures of Tang et al. and Cowsert, one of ordinary skill in the art would not have a reasonable expectation of success at

generating oligonucleotide compounds with higher levels of activity at substantially lower doses, as has been disclosed and claimed in the instant application.

Furthermore, the combination of Tang et al. and Cowsert do not teach oligonucleotide compounds capable of specifically hybridizing to a nucleic acid molecule encoding apolipoprotein B (SEQ ID NO: 3), excluding the start codon region as a target region. Moreover, neither Tang et al. nor Cowsert teach the reduction of apolipoprotein B (SEQ ID NO: 3) mRNA levels of at least 70%. As such, the combination of Tang et al. and Cowsert does not teach all of the claim limitations.

Accordingly, Claims 1-2, 4-14, 20, and 28 as amended herewith are unobvious over the combination of Tang et al. and Cowsert. For these reasons, the references fail to meet the standard of obviousness required under 35 U.S.C. 103(a) and Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 4, 2006

By: _____

Jerry L. Hefner
Registration No. 53,009
Attorney of Record
Customer No. 20,995
(619) 235-8550